Election/Restrictions

1. **Restriction is required under 35 U.S.C. 121 and 372.**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 2, 4-6, 9-10, 13, 15 and 20(in part), drawn to an isolated nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, an expression vector comprising said isolated nucleic acid molecule and a regulatory nucleic acid controlling the expression of the polypeptide encoded by said isolated nucleic acid molecule, a host cell genetically engineered to contain said expression vector, a transgenic non-human animal comprising said isolated nucleic acid, wherein the expression of said isolated nucleic acid molecule according to the SEQ ID NO's recited in Claim 1 is upregulated, and a pharmaceutical composition comprising said isolated nucleic acid.

Group 2, claim(s) 2-3, 5, 9-10, and 20(in part), drawn to an siRNA molecule targeted to an isolated nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, a host cell genetically engineered to contain said siRNA molecule, a non-human transgenic animal genetically engineered to contain said siRNA molecule in which the expression of said isolated nucleic acid molecule according to the SEQ ID NO's recited in Claim 1 is downregulated or absent, and a pharmaceutical composition comprising said siRNA molecule.

Group 3, claim(s) 12 and 16, drawn to an isolated polypeptide comprising an amino acid sequence substantially corresponding to one of the SEQ ID NO's recited in Claim 12.

Group 4, claim(s) 8, drawn to an antibody with specific reactivity to a nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1.

Group 5, claim(s) 14, drawn to an antibody specifically reactive with a polypeptide comprising an amino acid sequence substantially corresponding to one of the SEQ ID NO's recited in Claim 12.

Group 6, claim(s) 7 and 19(in part), drawn to a method of treating an angiogenesis-related condition comprising the step of administering an expression vector encoding a polypeptide encoded by a nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, wherein vasculogenesis or angiogenesis is enhanced or increased.

Group 7, claim(s) 7 and 19(in part), drawn to a method of treating an angiogenesis-related condition comprising the step of administering an expression vector encoding a polypeptide encoded by a nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, wherein vasculogenesis or angiogenesis is inhibited or decreased.

Group 8, claim(s) 19(in part), drawn to a method of treating an angiogenesis-related condition comprising the step of administering an expression vector encoding an siRNA targeted to a nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, wherein vasculogenesis or angiogenesis is enhanced or increased.

Group 9, claim(s) 19(in part), drawn to a method of treating an angiogenesis-related condition comprising the step of administering an expression vector encoding an siRNA targeted to a nucleic acid molecule according to one of the SEQ ID NO's recited in Claim 1, wherein vasculogenesis or angiogenesis is inhibited or decreased.

Group 10, claim(s) 11, 17 and 21, drawn to a method of affecting vasculogenesis or angiogenesis comprising administering a pharmaceutical composition comprising an isolated polypeptide comprising an amino acid sequence substantially corresponding to one of the SEQ ID NO's recited in Claim 12, wherein vasculogenesis or angiogenesis is enhanced or increased.

Group 11, claim(s) 11, 17 and 21, drawn to a method of affecting vasculogenesis or angiogenesis comprising administering a pharmaceutical composition comprising an isolated polypeptide comprising an amino acid sequence substantially corresponding to one of the SEQ ID NO's recited in Claim 12, wherein vasculogenesis or angiogenesis is inhibited or decreased.

Group 12, claim(s) 18, drawn to a method of detecting an angiogenesis-related transcript in a cell, the method comprising contacting a biological sample with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence according to one of the SEQ ID NO's recited in Claim 18.

2. The inventions listed as Groups 1-12 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons:

A 371 case is considered to have unity of invention only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression "special technical feature' means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. In the instant application, the nucleic acid molecules of Group 1 encode a polypeptide; whereas, the nucleic acid molecules of Group 2 encode an siRNA molecule. Those of ordinary skill in the art recognize that protein-coding nucleic acid molecules achieve distinctly different effects than siRNA encoding nucleic acids, i.e. enzyme replacement therapy as opposed to gene silencing. Thus, *a priori*, the nucleic acid molecules do not share the same or corresponding special technical feature. The Group 4 antibody recognizes a nucleic acid molecule; whereas, the Group 5 antibody recognizes a polypeptide. Thus, *a priori*, the claimed antibodies do not share the same or corresponding special technical feature.

3. In addition, each invention detailed above reads on patentably distinct inventions drawn to multiple SEQ ID Numbers. According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(A) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common property or activity. Although the chemical compounds are a common

structure in that they are nucleic acids (Group 1, Group 2) or are all proteins (Group 3) or all antibodies, etc… (Group 4, Group 5), the compounds are not regarded as being of similar nature because all of the alternatives do not share a common property or activity. Each of the nucleic acids consists of a unique nucleotide sequence, has a distinct melting temperature and a distinct specificity of hybridization.

MPEP §803 states that "If the search and examination of all the claims in an application can be made without serious burden, the Examiner must examine them on the merits, even though they include claims to independent or distinct inventions."

Polynucleotide molecules are now often claimed in a single application in a variety of complex formats, some of which may embrace multiple inventions, such as by reference to: the ATCC number of a deposited plasmid containing the polynucleotide molecule; arbitrary laboratory designations; function of the nucleic acid alone or in combination with a partial linear nucleotide sequence; a genus described in terms of homology, percent identity, or hybridization; and a genus (or subgenus) described by nucleic acid sequence with variable positions specified within the sequence listing.

The Office recognizes that it now requires significantly more computational time to run individual nucleotide sequence searches for examination purposes than in 1996, and there is significantly more pertinent prior art to consider. In addition, it currently takes more Office resources to correlate the claimed polynucleotide with the polynucleotide as defined in the prior art because it is increasingly common for both patent Applicants and prior art references to describe a polynucleotide molecule in different ways. Each of the nucleic acids also encodes for a protein having a distinct amino acid sequence and a distinct biological activity. Similarly, each of the antibodies consists of a distinct amino acid sequence and has a different binding specificity for a different biological molecule (nucleic acid or polypeptide). In the instant case a serious burden exists since each limitation, directed to a distinctly different SEQ ID NO encoding a functionally distinct nucleic acid product requires a separate, divergent, and non co-extensive search and examination of the patent and non-patent literature. A search for polynucleotides comprising SEQ ID NO: 2 would not be co-extensive with a search for polynucleotides comprising SEQ ID NO:14. Further, a reference rendering SEQ ID NO:7 as

anticipated or obvious over the prior art would not necessarily also render SEQ ID NO:41 as anticipated or obvious over the prior art.

In response to the restriction requirement, Applicant must further elect a single nucleic acid subgroup and/or the corresponding siRNA and/or the corresponding polypeptide encoded by said nucleic acid subgroup selected from the group consisting of:

a) SEQ ID NO:2 and SEQ ID NO:4,

b) SEQ ID NO:7 and SEQ ID NO:9,

c) SEQ ID NO:12 and SEQ ID NO:14,

d) SEQ ID NO:17, SEQ ID NO:19 and SEQ ID NO:21,

e) SEQ ID NO:24 and SEQ ID NO:26,

f) SEQ ID NO:29 and SEQ ID NO:31,

g) SEQ ID NO:34 and SEQ ID NO:36,

h) SEQ ID NO:39 and SEQ ID NO:41,

i) SEQ ID NO:44 and SEQ ID NO:46, and

j) SEQ ID NO:49 and SEQ ID NO:51.

It is further noted that this is a restriction requirement and should NOT be construed as an election of species.

Inventions 1-5 are directed to related products. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed have materially different design (siRNA vs. polypeptide vs. antibody), mode of operation and effect. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Inventions 6-12 are directed to related processes. The related inventions are distinct if: (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are

mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed have materially different design (protein-coding nucleic acid vs. siRNA), mode of operation and effect (enhance vs. inhibit). Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Inventions 1-5 and Inventions 6-12 are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the Groups 6-12 methods may be practiced with a multitude of distinctly different products, as evidenced by the claims.

The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting

rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and/or examination burden if restriction were not required because at least the following reason(s) apply:

A search for a protein-coding nucleic acid molecule would not be co-extensive with a search for a method of treating angiogenesis comprising the administration of an siRNA molecule. Further, a reference rendering an antibody specifically reacting to a first polypeptide as anticipated or obvious over the prior art would not necessarily also render an antibody specifically reacting to a first nucleic acid molecule as anticipated or obvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/

Examiner, Art Unit 1633